Outcomes in patients treated with laser interstitial thermal therapy for primary brain cancer and brain metastases

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Abstract

Laser interstitial thermal therapy (LITT) is an emerging modality to treat benign and malignant brain lesions. LITT is a minimally invasive method to ablate tissue using laser-induced tissue heating, and serves as both a diagnostic and therapeutic modality for progressive brain lesions. We completed a single-center retrospective analysis of all patients with progressive brain lesions treated with LITT since its introduction at our center in August of 2015. Twelve patients have been treated for a total of 13 procedures, of which 10 patients had brain metastases and 2 patients had primary malignant gliomas. Biopsies were obtained immediately prior to laser-induced tissue heating in 10 procedures (76.9%), of which 7 biopsies showed treatment-related changes without viable tumor. After laser ablation, 2 of 3 patients previously on steroids were successfully weaned on first attempt. The results of this analysis indicate that LITT is a well-tolerated procedure enabling some patients to discontinue steroids that may be effective for diagnosing and treating radiation necrosis and tumor progression.

Introduction

LITT is a minimally invasive neurosurgical method to ablate tissue using laser-induced tissue heating, and is an emerging diagnostic and therapeutic modality for progressive brain lesions. The risks of LITT include neurologic deficits related to ablation of eloquent tissues, treatment-related edema, intracranial hemorrhage, and wound infection. Thin laser fiber probes allow for safe access to the lesion in question, and biopsies can be obtained to help establish a diagnosis intraoperatively. Several barriers prevented its use in the central nervous system (CNS), particularly the ability to accurately and efficiently place laser fiber probes into the brain to monitor rising tissue temperatures spatially. The development of image-guidance platforms, including MRI thermography, allowed accurate targeting and monitoring of CNS lesions [1]. This thermography is crucial to allow heating of target neoplastic tissues to threshold temperatures for tissue death while limiting thermal injury to crucial CNS structures. This combination of surgical stereotactic laser fiber placement to thermally ablate tissues via LITT is an FDA-approved minimally invasive procedure. LITT was introduced as a diagnostic and therapeutic option at the University of Michigan in August of 2015. Given the relative novelty of the procedure, there is a paucity of data on the patient characteristics, clinical outcomes, toxicities, and correlations between pathologic and radiologic features in cancer patients who have undergone LITT for progressive brain lesions[2].

LITT provides a novel therapeutic opportunity for addressing both radiation necrosis as well as local tumor progression. Following focal high dose radiation, radiation-related treatment effects or radiation necrosis may be observed, which manifest as enlargement of the treated, contrast-enhancing lesion on standard MRI[3]. Treatment effects are difficult to distinguish from actual tumor progression, which has a similar appearance. The gold standard to distinguish between these two scenarios is biopsy; however, obtaining tissue previously required invasive craniotomy, for which a minority of patients are eligible. Therefore, there is a critically unmet need to identify noninvasive approaches for assessing patients with these imaging findings after treatment to establish an accurate diagnosis and guide optimal management.

Materials and Methods

We identified cancer patients who have undergone LITT when clinically indicated for treatment of progressive contrast-enhancing lesions at the University of Michigan Rogel Comprehensive Cancer Center since the procedure was introduced in August 2015. IRB approval was obtained. Demographic and clinical features were obtained for the study population.

Results

Insert Table 1

Twelve patients underwent LITT at our institution for a total of 13 procedures performed by 2 neurosurgeons. One patient underwent 2 LITT ablations on separate dates approximately 7 months apart for anatomically distinct lesions and locations. Of these 12 patients, 10 had brain metastases from solid malignancies and 2 had glioblastoma multiforme (GBM). Non-small cell lung cancer (NSCLC) was the most commonly treated histology (6 patients, 50%). The median age of patients on the day of the LITT procedure was 58.4 years and 66.7% of treated patients were female. All but 1 patient received focal radiation prior to LITT, and the majority of patients received multiple prior therapies. The most common site of LITT ablation was in the frontal cortex (7 procedures, 53.8%), and both supratentorial and infratentorial lesions were treated. Biopsy for intra-operative frozen section, followed by formal pathology review, was obtained in the majority of procedures (10 procedures, 76.9%) prior to laser-induced tissue ablation. Pathology revealed treatment effect in 7 cases and viable tumor in 3 cases.

Three patients were on steroids prior to LITT for a median duration of 70 days (range 7-83 days). Of those, 2 (66.7%) were able to taper off steroids during the initial attempt. All 9 additional patients were started on steroids after LITT per standard protocol and 6 were successfully weaned on initial steroid taper. The median duration of post-LITT steroids was 32 days with a range of 6 to 300 days. One patient was lost to follow-up and not included in this calculation. Reasons for failure of initial taper included seizure (grade 3) and worsening weakness (grade 2).

Focal motor weakness was the most common neurologic impairment after LITT in 4 patients, for which 3 patients required inpatient rehabilitation stays to regain function prior to discharge home. One of these patients had weakness prior to LITT and another had preceding ambulatory dysfunction. All 4 patients who developed weakness had lesions that were either in, immediately adjacent, or near the motor cortex or corticospinal motor tracts.

Of all patients who underwent LITT at our institution, 4 have subsequently died (33.3%), including one from unknown causes 8.1 months after LITT, one from pulmonary hemorrhage 27.4 months after LITT, and two from progression of intracranial disease 9.9 months and 19.4 months, respectively, after LITT.

Insert Table 2

Insert Supplemental Figure 1

Discussion

Our findings indicate that LITT is a well-tolerated procedure, allowing some patients to discontinue steroids, that may be effective for diagnosing and treating radiation necrosis and tumor progression. In the setting of suspected radiation necrosis, deciding between bevacizumab, LITT, or observation is complex. Patients selected for LITT were those for whom there was (1) increasing size of contrast enhancement, (2) diagnostic uncertainty between necrosis/treatment effects and recurrent tumor, (3) an increasing concern of the possibility of recurrence, and (4) progressive symptomatology.

Interpretation of post-LITT imaging remains an area of active research. Contrast enhancing volume increases after LITT on the 3-month post-op MRI and then gradually starts to decrease over the 6-month and one-year MRIs in patients who are responsive to LITT. Similarly, diffusion imaging shows initial increased diffusion restriction on DWI in the center of the lesion, likely due to the central area of necrosis of the lesion, and then diminishes over time.

The analysis is limited by sample size and its retrospective, single-institution design. Ultimately, well-designed randomized trials comparing treatment modalities are needed to further elucidate the efficacy and safety of this novel therapy.

References

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Table 1: Clinical and Demographic Features of 12 Patients Treated with LITT for Progressive Brain Lesions

		n	**%**
Patients		12*	
Male		4	33.3%
Female		8	66.7%
Median age in years at time of LITT (range)	58.4 (42.4 – 83.2)		
Primary Malignancy			
NSCLC		6	50%
Breast		2	16.7%
GBM		2	16.7%
Melanoma		1	8.3%
Colon Adenocarcinoma		1	8.3%
LITT Procedures		13	
Cumulative CNS Treatment Pre-LITT			
None		1	7.7%
Radiation alone		2	15.4%
Chemoradiation		1	7.7%
Resection + Radiation		2	15.4%
Resection + Radiation + LITT**(different location)**		1	7.7%
Resection + Chemoradiation		2	15.4%
Resection + Radiation + Immunotherapy		2	15.4%

Resection + Chemoradiation + Immunotherapy		1	7.7%
Resection + Chemoradiation + Bevacizumab		1	7.7%
Location of brain lesion treated by LITT			
Frontal		7	53.8%
Parietal		3	23.1%
Temporal		1	7.7%
Cerebellar		2	15.4%
Pathology of brain lesion obtained during LITT			
Viable Tumor		3	23.1%
Necrosis/Treatment effect		7	53.8%
No Biopsy		3	23.1%
Steroids Used Pre-LITT		3	23.1%
Tolerated Steroid Cessation Post-LITT		9	69.2%
Median duration of Steroids Post-LITT in days (range)	32 (6 – 300)**		
Cumulative CNS Treatment Post-LITT* **			
None		4	30.8%
LITT**(different location)**		1	7.7%
Immunotherapy		3	23.1%
Resection		1	7.7%
Chemotherapy + Bevacizumab		2	15.4%
Resection + Chemoradiation		1	7.7%

Resection + Chemoradiation + Immunotherapy		1	7.7%
Post-LITT Complications			
Focal motor weakness		4	30.8%
Infection		0	0%
Hemorrhage		0	0%

*: 13 lesions treated in 12 patients
**: Median calculated for 12 procedures, as 1 patient was lost to follow up
***: Treatment given for subsequent progression of disease during the course of follow up for this study

Table 2: Individual Patient Characteristics

Patient	Cancer Diagnosis	ECOG PS at Time of LITT	CNS Location	Pathology	Cumulative Pre-LITT Tx	Cumulative prior SRS dose to area treated with LITT	Time from most recent SRS to LITT	Cumulative Post-LITT Tx	Time to Next CNS-Tx for Progression	Neuro Symptoms Pre-LITT	Pre-LITT Steroids	Tolerated Post-LITT Taper	Alive
1	NSCLC	1	Cerebellum	Viable tumor	RXCI	18 Gy	13.3 months	R	5.3 months	Yes	Yes, Dex 4 mg PO BID x 7 days	Yes	No, OS 8.1 months from LITT
2	GBM	0	Frontal	Viable tumor	RXC	60 Gy	48.9 months	RXC	14.6 months	No	No	Yes	Yes
3	GBM	1	Frontal	Treatment effect	RXC	75 Gy	8.8 months	CB	14.6 months	Yes	No	No	No, OS 19.4 months from LITT
4	NSCLC	0	Temporal	No biopsy	N	N/A	N/A	RXCI	10 months	Yes	No	Yes	No, OS 27.4 months from LITT
5^	Breast invasive ductal carcinoma	0	Parietal	Treatment effect	RX	24 Gy	10.5 months	L	7.5 months	No	No	Yes	Yes
	Breast invasive ductal carcinoma	Not reported	Frontal	No biopsy	RXL	18 Gy	17.9 months	N	N/A	Yes	No	Yes	
6	NSCLC	Not reported	Cerebellum	Treatment effect	XC	44 Gy	27.8 months	N*	*	Yes	No	No*	*
7	Melanoma	1	Parietal	Treatment effect	X	20 Gy	15.8 months	I	N/A	Yes	No	Yes	Yes
8	NSCLC	Not reported	Parietal	Treatment effect	RXI	22 Gy	4.4 months	I	N/A	No	No	Yes	Yes
9	Colon adenocarcinoma	1	Frontal	No biopsy	RXCB**	18 Gy	16.6 months	CB**	N/A	Yes	Yes, Dex 1 mg PO	Yes	Yes

											daily x 70 days		
10	NSCLC	2	Frontal	Treatment effect	X	18 Gy	6.9 months	N	N/A	Yes	No	No	Yes
11	NSCLC	2	Frontal	Viable tumor	RX	22 Gy	12.0 months	N	N/A	Yes	Yes, Dex 4 mg PO BID x 83 days	No	No, OS 9.9 months from LITT
12	Breast invasive ductal carcinoma	1	Frontal	Treatment effect	RXI	30 Gy	10.2 months	I	N/A	Yes	No	Yes	Yes

R: Resection, C: Chemotherapy, X: Radiation, I: Immunotherapy, B: Bevacizumab, L: LITT, N: None
Dex: Dexamethasone; SRS: Stereotactic Radiosurgery; OS: Overall Survival
^: One patient underwent 2 LITT ablations on separate dates approximately 7 months apart for anatomically distinct lesions and locations
*: Lost to follow-up shortly after LITT procedure and declined further therapy
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